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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,693	01/19/2001	Daniel S. Sem	P-TB 4568	6461

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CAMPBELL & FLORES LLP
4370 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO, CA 92122

EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,693	SEM, DANIEL S.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-19 and 37-61* is/are pending in the application.

4a) Of the above claim(s) *15-19,37-41 and 57-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

NOTE the change of examiner in this application.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/21/03 has been entered.

2. The response filed on 11/21/03 has been fully considered and entered into the application. Claims 42, 47 have been amended by the amendment filed on 11/21/03.

3. Claims 15-19 and 37-61 are currently pending in this application.

4. Claims 15-19, 37-41 and 57-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 2/12/03.

Examiner has addressed the traversal in the response filed on 5/19/03 and made the restriction final. Thus applicants are requested to cancel the withdrawn claims.

5. Claims 42-56 are currently being examined in this application.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

In the specification e.g., in pages 11, 20, 21 and 22 hyperlinks are noted. Applicants are

requested to amend the specification by deleting the hyperlinks.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 42-56 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Briefly the instant claims are drawn to a method for identifying a bi-target ligand to enzymes in a enzyme family comprising:

A) identifying a first bi-ligand to a first enzyme in said enzyme family by i) attaching a linker to a common ligand to form a module; ii) generating a population of bi-ligands by attaching a second ligand to the module; iii) screening the population of bi-ligands for binding to an enzyme (binding to multiple receptors); iv) identifying a bi-ligand for binding to an enzyme in the family;

B) identifying a second bi-ligand (comprising common ligand and third ligand) to a second enzyme in the same family of enzymes by repeating steps I)-iv);

C) generating a bi-target ligand comprising a common ligand, second ligand and third ligand, which are attached to a linker.

According to the text of 35 USC sec. 101, an invention must be "useful". Our reviewing courts have applied the labels, "specific utility" (or "practical utility") to refer to this aspect of the "useful invention" requirement of sec. 101. (Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881, 883 (CCPA 1980)). In Nelson, the court characterized "specific utility" (or "practical utility") as "a shorthand way of attributing real-world value to claimed subject matter. In other words, one

skilled in the art can use a claimed discovery in a manner, which provides some immediate benefit to the public." (Id. at 856.)

The bi-target ligand (common ligand, specificity ligand and third ligand linked via linker) to enzyme and the population of bi-ligands (common ligand – linker – specificity ligand) of the claimed method are not supported by a specific asserted utility and do not, without further research and experimentation, provide an immediate benefit to the public. Rather, the bi-target ligand and/or bi-ligand comprise compounds , which are yet to be tested for their therapeutic activity. For example, the instant specification, in page 46 discloses that the bi-ligand can be validated as a likely effective therapeutic agent (if the target receptor is a pathogenic organism, the bi-ligand can be tested for inhibitory activity in the target organism). Thus, the bi-ligands have to be further tested for activity. Thus, any benefit to the public (to one of ordinary skill in the art) is speculative. There is no basis in the specification upon which to conclude that *any* of the compounds encompassed by bi-target or the bi-ligand of the instant claims **are**, or will turn out to be, biologically active after testing. In the specification, applicant implies that once at least two bi-ligands exhibiting specificity are identified, the two bi-ligands are combined to form the bi-target ligand having specificity to two different members of the receptor family. Thus, the therapeutic use of the bi-target ligand is to take place at some future time, only when the properties of the bi-ligands have been elucidated by the experimental methods (screening assays). Absent a disclosure of those properties, the asserted utility of therapeutic use lacks specificity.

The instant specification discloses that the bi-ligands (common ligand – linker – specificity ligand) and bi-target ligands act as therapeutic agents. A "specific utility" is specific

to the subject matter claimed. This is contrast with a general utility that would be applicable to the broad class of invention. Indicating the compound may be useful in treating a disorder (bacterial infection) or has useful biological properties would not be sufficient to define specific utility of the compound (e.g., see MPEP 2107.01). Further the specification has not shown the correlation between the similar known compounds, which have established utility and/or data from in vivo or in vitro testing of the compounds to support the therapeutic utility.

Note, because the claimed invention is not supported by a specific asserted utility for the reasons just set forth, credibility cannot be assessed.

This is not to say that inventions that are to be used exclusively in a research setting (i.e., research tools) always lack a specific asserted utility. Indeed, many research tools such as telescopes, gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility. (See USPTO Utility Guidelines, page 12.) However, inventions that have a specifically identified utility must be distinguished from those whose utility requires further research to identify or reasonably confirm. (Id.) Research tools (such as gas chromatographs, screening assays, etc.) are useful in the sense that they can be used in conjunction with other method steps to evaluate materials other than themselves or to arrive at some result. The bi-ligands (common ligand – linker – specificity ligand), and bi-target ligands (common ligand, specificity ligand and third ligand linked via linker) of the instant claims are not research tools in this sense. Rather, they are themselves the subject of basic research, whose usefulness or lack thereof has yet to be established. (e.g., see specification page 46.) Merely labeling the instant libraries as "research tools" does not impart the specific utility required by this statute.

In the absence of an asserted specific utility, the "useful" requirement may be established by reference to a well established utility. A "well established utility" is a "specific utility" which is well known, immediately apparent and implied by the specification based on the disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. The bi-ligands (common ligand – linker – specificity ligand), and bi-target ligands (common ligand, specificity ligand and third ligand linked via linker) of the instant claims are not supported by a well established utility, however, because neither the specification as filed nor any art of record discloses or suggests any property or activity for the compounds such that another non-asserted utility would be well established for the compounds. Further, the compounds of the instant claims are not recognizable as analogous to compounds with a recognized pharmacological (or other) activity. In the absence of any data as to their activity, there is no basis upon which to base either a specific or a well-established utility.

Claims 42-56 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 42-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a "method for identifying a bi-target ligand (common ligand, specificity ligand and third ligand linked via linker) to enzymes in an enzyme family". The identified "bi-target ligand" is made up of three parts: a "common ligand", a "second ligand" and a "third ligand". The claims use generic terminology such as "cofactor or mimic thereof", "second ligand", "third ligand", "substrate binding site", "enzyme family" and "linker". These terms are defined/discussed in the instant disclosure but the definitions are very broad and open-ended.

No specific structure of the identified "bi-target ligand" is set forth and no specific "method for identifying a bi-target ligand" is described in the instant disclosure. The exemplary figure 3 of the instant specification does not show the structure of the ligands. The present application fails to describe a specific example of identifying even a single compound, which is within the scope of the presently claimed invention. Applicant's claimed scope represents only an invitation to experiment regarding possible identified "bi-target ligands" within the scope of the claims.

The instant claims give ***no structure*** for the entities that make up the identified "bi-target ligands" ("common ligand"/"cofactor or mimic thereof", "second/third ligand[s]" and "linker") and no structural information as to how they are to be linked together to form such "bi-target

ligands". Thus the claims could encompass an infinite number of variations. Note that "the essential goal of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978). Another objective is to put the public in possession of what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything that is in common use, or already known. *Evans v. Eaton*, 20 U.S. (7 Wheat.) 356 (1822).

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires representative examples, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure.

Again, the specification discloses **no** examples of the preparation and use of such "bi-target ligands". These compounds (i.e. "common ligand"/"cofactor or mimic thereof", "second/third ligand[s]" and "linker") could encompass very different moieties of widely varying structures. No specific structure of the identified "bi-target ligand" or bi-ligand used

in the claimed invention is set forth in the specification. Thus, the disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members, which are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

11. Claims 42-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Briefly the instant claims are drawn to a method for identifying a bi-target ligand to enzymes in an enzyme family comprising:

A) identifying a first bi-ligand to a first enzyme in said enzyme family by I) attaching a linker to a common ligand to form a module; ii) generating a population of bi-ligands by attaching a second ligand to the module; iii) screening the population of bi-ligands for binding to an enzyme (binding to multiple receptors); iv) identifying a bi-ligand for binding to an enzyme in the family;

B) identifying a second bi-ligand (comprising common ligand and third ligand) to a second enzyme in the same family of enzymes by repeating steps I)-iv);

C) generating a bi-target ligand comprising a common ligand, second ligand and third ligand, which are attached to a linker.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement

and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: The claims are drawn to a "method for identifying a bi-target ligand" where the "bi-target ligand" is made up of three parts: a "common ligand", a "second ligand" and a "third ligand", and "a linker." No limitations on the specific structure of the identified "bi-target ligand" or 'bi-ligands' are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention. For example, the "common ligand" and "second and third ligands" must bind to their respective sites and the sites must be able to be determined.

The state of the prior art and the level of predictability in the art: Compounds that interact with various enzyme targets were known in the art at the time of filing; however, only limited numbers of such compounds were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of *any* such compound. The identified "bi-target ligands" of the instant claims require "common ligands" and "second and third ligands"; however, such trimeric ligands for enzyme families were not generally known in the art. The structures of possible variants are sufficiently diverse

and one of ordinary skill would not be able to predict their structures. Moreover, the claims require the presence of a "common ligand" which is a "cofactor " or is a "cofactor mimic" and two additional ligands that bind to "substrate binding sites" of a first and a second enzyme in an "enzyme family". One of ordinary skill would not know, *a priori*, how to determine the structure of such ligands because the determination of the different binding sites in an "enzyme family" would be unpredictable. Applicant's claimed scope of compounds represents only an invitation to experiment regarding possible methods of identification of undefined "bi-target ligands" (see also above rejection concerning written description and cases cited therein).

The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

The existence of working examples and the quantity of experimentation needed to make or use the invention based on the content of the disclosure: Applicants have provided **no** working examples and the state of the prior art is such that one of ordinary skill could not predict how to determine and then link the various moieties that make up the identified "bi-target ligand" as required by the instant claims. Therefore, further research would be necessary to make or use the invention and it would require undue experimentation to carry out the invention as claimed. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23,

20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the invention would require undue experimentation.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claims 42-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite 'can bind' which is vague and indefinite. Applicants are requested to amend the claims.

Response to Arguments

14. Applicant's arguments filed on 9/18/03 (after final) with respect to claims 42-56 have been considered but are moot in view of the new ground(s) of rejection.

And further the written description rejection and the enablement rejection have been addressed in the advisory action.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Flex Schedule can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
12 March 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER